

REMARKS

The present application is directed to a method of detecting the presence of a target nucleic acid in a sample. Claims 43-71 and 85-86 are under examination in the application. Claims 45, 59, 65 are amended in this Second Amendment and Response to Office Action. No new matter is added.

Maintained Rejection under 35 U.S.C. §102(e)

The Examiner maintains the rejection of Claims 43-44, 48-55, and 57-69 under 35 U.S.C. §102(e) as anticipated by US 2004/0241679. Applicant respectfully traverses this rejection.

Applicant respectfully maintains the position that US 2004/0241679 fails to disclose a method using a DNA duplex binding agent as the acceptor, wherein the DNA duplex binding agent is selected on the basis that its emissions are not detectable in the context of the method. Because Lee does not disclose each and every element of the claims of the present application, as currently pending, it fails to anticipate the claims.

The Examiner asserts in section 5 on pages 3 and 4 of the Office Action, that, although US2004/0241679 relates to systems in which a FRET assay is used, the document also suggests the possibility of measuring fluorescence from only the acceptor. The Examiner then asserts that, based on the above suggestion, a person of ordinary skill in the art in the field of the present application would understand that measurement of signal from only the donor would be possible.

Applicant respectfully brings to the Examiner's attention that "[t]o anticipate a claim, the reference must teach every element of the claim." See MPEP 2131. The Examiner rejects the claims as anticipated by US2004/0241679. However, the cited reference does not teach each and every element of the claim, as required for anticipation. Applicant asserts that that US2004/0241679 fails to anticipate the rejected claims and that

any inference that might be drawn by one of ordinary skill in the art in relation to the disclosure of reference is not relevant to the issue of anticipation.

US2004/0241679 discloses measurement of the strand-specific signal and specifies that this is the measurement of the signal provided by the acceptor moiety, as the Examiner states in the Office Action in reference to paragraph 0045 in US2004/0241679. This is not the same as a disclosure of measurement of the signal from the donor moiety. Indeed, the language used in US2004/0241679 is very clear that measurement of the signal from the donor moiety would not be suitable, with paragraph 0045 stating: “A simple measurement of the **strand specific** signal alone (**i.e.** that provided by the **acceptor** moiety) ...” (emphasis added).

Thus, US2004/0241679 fails to disclose a method using a DNA duplex binding agent as the acceptor, wherein the DNA duplex binding agent is selected on the basis that its emissions are not detectable in the context of the method, and fails to disclose, as required for anticipation, each and every element of independent Claims 43 and 66 and any of their dependent claims. Therefore, a rejection under 35 U.S.C. § 102(e) is improper. Applicant respectfully requests withdrawal of the rejection.

Maintained Obviousness-Type Double Patenting Rejection

The Examiner provisionally rejects Claims 43-44 and 48-69 on the grounds of nonstatutory obviousness-type double patenting over Claims 1-4, 6-7, 9, and 10-14 of co-pending U.S. Patent Application Serial No. 10/478,788 (published as US2004/0241679). Applicant respectfully traverses the rejection. Applicant maintains that, as previously stated, the cited claims of U.S. Patent Application Serial No. 10/478,788 fail to disclose or suggest any dark quenchers that may act as DNA duplex binding agents. The “label” recited in the cited claims forms an element of the signalling system other than DNA duplex binding agents – i.e., the label fixed to the probe.

On page 5 of the Office Action, the Examiner discusses Claim 9 of US2004/0241679. Contrary to the Examiner's assertion, Claim 9 refers to the "acceptor label" being a "dark acceptor" and not a DNA duplex binding agent as stated by the Examiner. Applicant asserts that the cited claims of U.S. Patent Application Serial No. 10/478,788 fail to render obvious the rejected claims of the present application. Applicant respectfully submits that the pending claims are therefore patentably distinct from the cited claims of the co-pending U.S. Patent Application Serial No. 10/478,788. Accordingly, applicant respectfully requests withdrawal of the rejection.

New Grounds for Rejection under 35 U.S.C. §112, second paragraph

The Examiner rejects Claim 86 under 35 U.S.C. §112, second paragraph, as indefinite. The Examiner asserts that Claim 86 recites a limitation essentially similar to a limitation in base Claim 66. Applicant respectfully submits that the amendments to the claims overcome the rejection. Claim 66 has been amended to correspond to Claim 43, as previously presented. Applicant asserts that the amendments overcome the rejection, and requests its withdrawal.

New Grounds for Rejection under 35 U.S.C. §102(b)

The Examiner rejects Claims 43-44 and 48-69 under 35 U.S.C. §102(b) as anticipated by International Patent Publication WO 99/28500. Applicant respectfully traverses the rejection.

"To anticipate a claim, the reference must teach every element of the claim." *See* MPEP 2131. Applicant respectfully asserts that that WO 99/28500 fails to teach each and every element of Claims 43-44 and 48-69 and fails to anticipate the claims. Specifically, WO 99/28500 fails to discuss a method wherein the DNA duplex binding agent does not emit visible light. Furthermore, WO 99/28500 fails to discuss a method wherein the DNA duplex binding agent can absorb energy from the fluorescent label on the probe but the emissions of the DNA duplex binding agent are not detectable in the context of the method.

The Examiner found the foregoing arguments persuasive when submitted in the First Amendment and Response filed in the present application, as stated on pages 2-3 of the Office Action. Accordingly, applicant requests withdrawal of the rejection of Claims 43-44 and 48-69 under 35 U.S.C. §102(b) because WO 99/28500 fails to teach each and every element of the rejected claims.

Furthermore, on page 7 of the Office Action, the Examiner states that, on page 11, “Lee discusses the embodiment where the donor and acceptor do not have overlapping wavelengths[,] and measurement can take place by measuring the emissions from one of the labels at a particular wavelength.” In fact, page 11 lines 11-15 of WO 99/28500 merely hypothesizes that “[p]referably, the molecules used as donor and/or acceptor produce sharp peaks, and there is **little or no** overlap in the wavelengths of the emission. Under these circumstances, **it may not be necessary** to resolve the strand specific peak from the DNA duplex binding agent signal” (emphasis added). WO 99/28500 goes on to speculate that “The ethidium bromide/fluorescein combination **may** fulfil this requirement.” Applicant asserts that WO 99/28500 merely discusses a goal to be aimed at, and does not teach each and every element of the pending claims as required for anticipation.

Furthermore, the Examiner asserts on page 7 of the Office Action that “one of skill could reason that the embodiment also included measuring only emission from fluorescein. In this case, the emissions from EtBr are not detectable in the context of the method” (emphasis added). Applicant brings to the Examiner’s attention that, for anticipation, the reference must teach each and every element of the claims. *See* MPEP 2131. Applicant asserts that WO 99/28500 fails to teach each and every reference of the claims rejected by the Examiner. Applicant respectfully submits that inference that could be drawn by one of ordinary skill in the art through reasoning in relation to the disclosure of reference does not provide the teaching necessary for anticipation.

Moreover, applicant asserts that one of ordinary skill in the art in the field of the present application, at the priority date of the present application, would understand that

the section WO 99/28500 cited by the Examiner fails to disclose an operable embodiment of a system for measuring the emissions from one of the labels due to the “leakage” of the signals between the fluorescent molecules, as discussed in more detail in the following section of this Response. The “leakage” problem is discussed on page 3, lines 13-21 of the present application.

In view of the foregoing, Applicant asserts that WO 99/28500 fails to anticipate Claims 43 and 66 or any of their dependent claims. Applicant therefore requests withdrawal of the rejection of Claims 43-44 and 48-69 under 35 U.S.C. §102(b) as anticipated by an International Patent Publication WO 99/28500.

New Grounds for Rejection under 35 U.S.C. §103(a)

Rejection over International Publication WO 99/28500 in view of Smith et al.

The Examiner rejects Claims 45-47, 66-71 and 85-86 under 35 U.S.C. §103(a) as obvious over International Publication WO 99/28500 in view of Smith et al., “Mitoxantrone-DNA binding and the induction of Topoisomerase II associated DNA Damage in Multi-Drug Resistant Small Cell Lung Cancer Cells.” *Biochemical Pharmacology* (1990), v. 40, pp. 2069-2078 (“Smith”). Applicant respectfully traverses the rejection.

When characterizing the teaching of WO 99/28500 in this section of the Office Action, the Examiner interprets the reference as applied in the rejection under 35 U.S.C. §102(b). As set forth above, applicant asserts that, contrary to what the Examiner asserts, the hypothetical discussion on page 11 of WO 99/28500 merely states a goal to be achieved. This is clear from the conditional language used in WO 99/28500. In fact, at the priority date of the present application, it had been found that there was sufficient “leakage” in the signal, when highly fluorescent donors and acceptors, such as ethidium bromide and fluorescein, were used, and that it was not generally possible to measure only one of the signals and obtain accurate results. Therefore, contrary to the Examiner’s assertion, an

ethidium bromide signal will always be detectable to some extent, in the context of the method.

The “leakage” of the signals between the fluorescent molecules is set out as a part of the problem to be solved, on page 3, lines 13-21 of the present application. MPEP 2142 states: “To reach a proper determination under 35 U.S.C. §103, the examiner must step backward in time and into the shoes worn by the hypothetical ‘person of ordinary skill in the art’ when the invention was unknown and just before it was made. In view of all factual information, the examiner must then make a determination whether the claimed invention ‘as a whole’ would have been obvious at that time to that person.” Thus, the development of knowledge after the publication date of an item of prior art must be taken into account when assessing the teaching provided to the skilled person by the prior art at the priority date of an application. Applicant has taken care to describe, in the background of the application, the known difficulties with the prior art, so as to fully delineate the differences between the claimed invention and the prior art and the advantages provided by applicant’s discovery. Claimed embodiments of applicant’s invention resolve the previously unresolved problem. Based on the teaching of WO 99/28500, the solution, as set forth in the claims, as a whole, would not have been obvious to one of ordinary skill in the art at the priority date of the present application.

The teaching of WO 99/28500 with regard to this unresolved problem is that one should seek pairs of donor and acceptor molecules that each produce “sharp peaks” and have “little or no overlap in emissions”. In contrast, applicant discovered that, to resolve the previously unresolved problem of signal “leakage,” it is important to focus on the selection of, specifically, suitable DNA duplex binding agents to achieve the desired result. This is a fundamentally different approach to the problem from that disclosed in WO 99/28500. Applicant’s approach is not taught or suggested in WO 99/28500. Thus, WO 99/28500 fails to render obvious the claimed embodiments of applicant’s invention.

The teachings of Smith fail to remedy the deficiencies of WO 99/28500. First, Smith is a paper in a different scientific field. It is concerned with the DNA-binding activity of mitoxantrone in the context of its therapeutic activity and, in particular, how it interacts with tumour cells. The purpose of the fluorescent labelling is to allow the detection of the position of the mitoxantrone in a cell. Hence, one of ordinary skill in the art in the field of the present application, when reading WO 99/28500 and seeking an alternative reagent set for use in detecting PCR reactions, is unlikely to consider Smith.

Furthermore, even if one of ordinary skill in the art were to consider Smith in order to resolve the problems delineated in WO 99/28500, the teachings of Smith would be rejected, since the members of the reagent pair used are both effectively DNA binding agents (the fluorescent dye used, Ho33342 is described as a “DNA specific ligand”) and, clearly, such a combination would not operate in a system where some sequence specificity is required, as in the method recited in the rejected claims. Accordingly, combining the teaching of WO 99/28500 and Smith, as suggested by the Examiner, would result in an inoperable method.

At best, Smith discloses that mitoxantrone can quench fluorescence from Ho33342 labelled cells. The Examiner suggests that one of ordinary skill in the art in the field of the present application would be motivated to replace the acceptor used in WO99/28500 with mitoxantrone. Applicant respectfully disagrees with this premise. In fact, the teaching of WO99/28500 is that it is preferable to use measurement of both donor and acceptor signals (see page 10, lines 19-26). However, if one were to be trying to measure a single signal only, this should be done by seeking pairs of compounds with “sharp peaks” of fluorescence, as outlined above. There is nothing in Smith that suggests this is a feature of mitoxantrone, since Smith is silent as to whether mitoxantrone has any kind of peak of fluorescent signal. Therefore, at the priority date of the present application, one of ordinary skill in the art would not have considered the option of replacing the acceptor species with a compound such as mitoxantrone, as suggested by the Examiner.

In view of the foregoing arguments, applicant respectfully asserts that WO 99/28500 in combination with Smith fails to render Claims 45-47, 66-71 and 85-86 obvious. Applicant requests withdrawal of the rejection.

Rejection over US 2004/0241679 in view of Smith

The Examiner rejects Claims 45-47, 66-71 and 85-86 under §103(a) as obvious in view of US 2004/0241679 in view of Smith. Applicant respectfully traverses the rejection.

Applicant respectfully asserts that US 2004/0241679 cannot be used to support a rejection under 35 U.S.C. §103(a). US 2004/0241679 qualifies as prior art only under 35 U.S.C. §102(e), as stated on page 12 of the Office Action. Applicant asserts that US 2004/0241679 cannot preclude patentability of the pending claims for reasons of obviousness due to the provisions of 35 U.S.C. §103(c), because U.S. Patent Application Serial No. 10/478,788, published as US2004/0241679, is commonly owned with the present application. *See* MPEP 706.02(l)(1).

35 U.S.C. §103 provides in the relevant section:

(C) Subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Applicant respectfully submits that US 2004/0241679 and the present application **were commonly owned** at the time the claimed embodiments of the invention of the present application were made. To disqualify prior art under 35 U.S.C. 103(c), applicants need to supply evidence that the invention described in the application for patent and the invention described in the "prior art" reference applied against the application were commonly owned by, or subject to an obligation of assignment to, the same person, at the time the invention in the application for patent was made. Applications and references will

be considered by the Examiner to be owned by, or subject to an obligation of assignment to the same person, at the time the invention was made, if the applicant(s) or an attorney or agent of record makes a statement to the effect that the application and the reference were, at the time the invention was made, owned by, or subject to an obligation of assignment to, the same person. Thus, a statement, by itself, will be sufficient evidence. (See MPEP 706.02(l)(2)).

In view of the foregoing, applicant respectfully asserts that a rejection under §103(a) as obvious in view of US 2004/0241679 in view of Smith is improper and request its withdrawal.

New Grounds for Obviousness-Type Double Patenting Rejection

The Examiner rejects Claims 43-46 and 48-70 on the grounds of nonstatutory obviousness-type double patenting over Claims 1-2, 4-9 and 11-13 of U.S. Patent No. 6,833,257 in view of Smith. Applicant respectfully traverses the rejection.

Applicant respectfully submits that, under the judicially created doctrine of obviousness-type double patenting, the rejected claims are patentably distinct from Claims 1-2, 4-9 and 11-13 of U.S. Patent No. 6,833,257 in view Smith at least because the emissions of the DNA duplex binding agent, recited in the claims of U.S. Patent No. 6,833,257, are not detectable in the context of the method of the present application, as recited in the pending claims. The basis of the method described in the present application is that the DNA duplex binding agent is an acceptor, specifically selected so that during the course of the method it does not emit a signal, which interferes with that of the label. The cited claims of U.S. Patent No. 6,833,257 do not teach or suggest such compounds or a description of how to use them in the method recited in the rejected claims.

The teaching of mitoxantrone in Smith does not remedy the deficiency of the cited claims of U.S. Patent No. 6,833,257 at least for the reasons discussed in above in the

section addressing the rejection of claims under 35 U.S.C. §103(a) over International Publication WO 99/28500 in view of Smith.

It is noted that U.S. Patent No. 6,833,257 was granted on the basis of the U.S. Patent application derived from International Publication WO 99/28500. Accordingly, applicant asserts that Claims 1-2, 4-9 and 11-13 of U.S. Patent No. 6,833,257, separately or when taken in view of Smith, do not render obvious pending Claims 43-46 and 48-70. Claims 43-46 and 48-70 are therefore patentably distinct from the cited claims of U.S. Patent No. 6,833,257. Applicant requests withdrawal of the rejection.

CONCLUSION

This response fully addresses the rejections in the Office Action of July 25, 2008. In light of the above remarks, applicant respectfully asserts that the application is now in condition for allowance. Such action is respectfully requested.

If the Examiner believes any informalities remain in the application that may be corrected by Examiner's Amendment, or if there are any other issues that can be resolved by telephone interview, a telephone call to the undersigned agent at (404) 815-6102 is respectfully solicited. No additional fees are believed due; however the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account number 11-0855.

Respectfully submitted,

/elena s. polovnikova/

By: Elena S. Polovnikova
Patent Agent
Reg. No. 52,130

KILPATRICK STOCKTON LLP
Suite 2800
1100 Peachtree Street
Atlanta, Georgia 30309-4530
Telephone: 404-815-6500
Facsimile: 404-541-3435
Our Docket: 41577-314737 (P205)